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EXAMINER	
HAMUD, FOZIA M	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 11/12/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/028,374	FEDER ET AL.	
	Examiner	Art Unit	
	Fozia M Hamud	1647	

-- The MAILING DATE f this communication app ars on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 August 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disp sition of Claims

4)☒ Claim(s) *24-43* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *24-43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 7/02
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 8/03 8/03
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Detailed Action

1. Receipt of Applicants' amendment filed on 18 August 2003, is acknowledged. Claims 1-23 have been canceled and new claims 24-43 have been added. Thus claims 24-43 are pending and under consideration.

Election/Restriction:

2. Applicant's election without traverse of the invention of Group I (canceled claims 1-4, 8-9 and 14-19), drawn to an isolated nucleic acid, an expression vector, a recombinant host cell and a method of producing the encoded protein, is acknowledged. The requirement is still deemed proper and is therefore made FINAL.
New claims 24-43 are drawn to the elected invention.

Specification:

3. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Information Disclosure Statement:

4a. References AR, AS, AT, AA and AB, cited on the PTO-1449 form submitted by Applicants on 22 July 2003 have not been considered, because they do not comply with 37 CFR 1.98(a)(2) requirements, since they fail to identify each publication by author and publication date. Applicant is advised that the date of submission of any item of information or any missing element(s) will be the date of submission for purposes of

determining compliance with the requirements based on the time of filing the IDS, including all "statement" requirements of 37 CFR 1.97(e). See MPEP § 609 ¶ C(1).

4b. References AR, AS, AT, 2AA, 2AB, 2AC, 2AD, 2AE, 2AF, 2AG and 2AH, cited on the PTO-1449 form submitted by Applicants on 18 August 2003 have not been considered, because the copies of these references have not been filed.

Claim Rejections - 35 U.S.C. § 101/112:

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

5a. Claims 24-43 of the instant invention are directed to an isolated nucleic acid encoding a polypeptide that comprises of amino acid residues 1-449, 2-449 of SEQ ID NO:2, an isolated nucleic acid consisting of the nucleotide sequence set forth in SEQ ID NO:1, a vector comprising said nucleic acid, a recombinant host cell comprising said vector and a method of producing the encoded protein.

The specification describes the claimed nucleic acid as encoding a polypeptide that has significant homology at the amino acid level to a number of leucine-rich repeat containing proteins, which include the human caspase recruitment protein 7, (the human NOD caspase recruitment protein 4 and the human cryopyrin protein, (see page 20, lines 21-33). The instant specification states that the protein of the instant invention was determined to be about 35% identical and 48% similar to the human caspase recruitment protein 7, and about 25% identifcal and 38% similar to human NOD caspase 4 protein and 51.7% identical and 64% similar to the human cryopyrin protein,

(see page 21, line 34 to page 22 line 8). The specification also states that analysis of the protein of the instant invention indicates that it contains a canonical LLR domain in the carboxy terminal, that is also shares cystiene rich regions on both sides of the LLR , domain, (page 22, lines 10-25). The protein of the instant invention is also described as not having a signal sequence, and that it contains only one transmembrane and that it is mainly expressed in the bone marrow and may function in the regulation of cell death during hemopoetic differentiation, (also page 22). The specification also speculates that the polypeptide of the instant invention is expected to share at least some biological activity with the leucine-rich repeat containing proteins found in the bone marrow cells and tissues and preferably to caspase recruitment protein family that contain pyrin domains, (page 23, lines 14-20). Instant specification also asserts that the claimed nucleic acid and the encoded polypeptide can be used to detect, treat, prevent diseases ad disorders related to aberrant apoptosis regulation, disorders related to aberrant cell adhesion regulation and disorders related aberrant cellular proliferation, (page 24, lines 9-15).

However, beyond making the above assertions, instant specification does not disclose any information regarding physiologic or functional characteristics of the protein encoded by the claimed nucleic acid. Furthermore, the polypeptide encoded by the claimed nucleic acid has never been expressed, no biological activity was assayed or determined for it, and only a deduced amino acid sequence and general methods of expressing recombinant proteins are disclosed.

While, the instant specification asserts that the polypeptide encoded by the claimed nucleic acid can be used therapeutically, and discloses conventional protein and nucleic acid administration techniques, it does not disclose specific diseases which can be treated or diagnosed using the claimed nucleic acid or the encoded polypeptide. Although instant specification asserts that the claimed nucleic acid and the encoded polypeptide might be used to detect, treat or prevent diseases ad disorders related to aberrant apoptosis regulation, disorders related to aberrant cell adhesion regulation and disorders related aberrant cellular proliferation, it does not establish a nexus between the claimed nucleic acid or the encoded polypeptide and any disease or disorder. Thus, the specification establishes no connection between any physiological condition and the protein of the instant invention, i.e, is the claimed nucleic acid or the encoded polypeptide over expressed, under expressed or completely lacking in any disorder? The specification provides no working examples as to the activity of the polypeptide encoded by the claimed nucleic acid, and one of ordinary skill in the art would not be able to predict what activity would be possessed by the protein. Therefore, one of ordinary skill in the art would not be able to predict the activity or physiological importance of the polypeptide encoded by the claimed nucleic acid. The fact that the claimed nucleic acid encoded a protein that shares identity to leucine-rich repeat containing proteins and may contain certain domains, does not provide utility for the claimed nucleic acid, because, the physiological role of the claimed nucleic acid or the encoded polypeptide has been not disclosed by Applicants. The claimed nucleic acid can't be used to diagnose any disorder, because instant specification does not establish

a link between the claimed nucleic acid and any disorder. For example, is there a reduction or over-production of said the claimed nucleic acid or the encoded polypeptide, relative to control tissues? Furthermore, no meaningful information will be obtained from tracking the level or the site of expression of the polypeptide encoded by the claimed nucleic acid, because there is no physiological or biological significance attached to these nucleotides or the encoded proteins.

The claimed invention is directed to a nucleic acid of as yet undetermined function or biological significance, therefore, unless Applicants demonstrate the physiological significance or the biological role of the instant nucleic acid and the protein it encodes or a correlation to a disease state, the claimed invention is not supported by either a specific and substantially asserted utility or a well established utility.

5b. Claims 24-43 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a substantially asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention. The instant specification does not define the physiological role of the polypeptide encoded by the claimed nucleic acid, neither does it establish a link between the claimed nucleic acid or the encoded protein and a physiological condition or disorder. Therefore, there is no specific and substantial asserted utility or well established utility for the claimed nucleic acid or the encoded protein. The specification discloses only the sequence of the claimed nucleic acid and the encoded protein, and that is insufficient to establish a specific or substantial utility for the claimed invention.

Should Applicants establish an activity for the polypeptide of SEQ ID NO:2 encoded by the nucleic acid, instant specification would still fail to adequately describe and enable an isolated nucleic acid that encodes a polypeptide having 80% to the polypeptide of SEQ ID NO: 2, an isolated nucleic acid comprising 80% to the nucleotide sequence of SEQ ID NO:1 . Applicants do not teach which regions of the polypeptide of SEQ ID NO:2, are critical for the functional and structural integrity of the polypeptide. The specification does not provide the requisite examples nor a representative number of different sequences that would allow the skilled artisan to produce an isolated nucleic acid that encodes a polypeptide having 80% to the polypeptide of SEQ ID NO: 2 of the polypeptide of SEQ ID NO:2, wherein said polypeptide retains the desired activity, nor does the disclosure provide criteria that explicitly enable such critical features. There is no guidance in the specification as to how one of ordinary skill in the art would generate a nucleic acid or a polypeptide encoded thereby, other than that exemplified. The issue here is the breadth of the claims in light of the predictability of the art as determined by the number of working examples, the skill level of the artisan and the guidance presented in the instant specification and the prior art of record.

In summary, the amount of experimentation required for one of ordinary skill in the art to use the invention recited in claims 39 and 43, an isolated nucleic acid that encodes a polypeptide having 80% to the polypeptide of SEQ ID NO: 2, nor an isolated nucleic acid comprising 80% to the nucleotide sequence of SEQ ID NO:1, that displays that desired activity, would be undue. To practice the instant invention in a manner consistent with the breadth of the claims would not require just a repetition of the work

consistent with the breadth of the claims would not require just a repetition of the work that is described in the instant application but a substantial inventive contribution on the part of a practitioner which would involve the determination of those nucleotide sequences of the disclosed naturally-occurring nucleic acid, which are required for functional and structural integrity of the claimed nucleic acid. It is this additional characterization of the disclosed nucleic acid that is required in order to obtain the functional and structural data needed to permit one to produce a nucleic acid which meets both the structural and functional requirements of the instant claim that constitutes undue experimentation.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6.. Claims 24, 29, 36-37 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

Claim 24 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. It is apparent that clone contained ATCC Deposit No: PTA-2676 is required to practice the claimed invention. As such the clone must be readily available or obtainable by a repeatable method set forth in the specification, or

otherwise readily available to the public. If the clone is not so obtainable or available, the requirements of 35 U.S.C. 112, first paragraph, may be satisfied by a deposit of the clone with the ATCC Deposit No: PTA-2676.

The specification, provides an ATCC accession number for the clone, however, the specification lacks complete deposit information for the deposit of the clone. If a deposit was made under the terms of the Budapest Treaty, then an affidavit or declaration by Applicants, or a statement by an attorney of record over his or her signature and registration number, stating that the instant invention will be irrevocably and without restriction released to the public upon the issuance of a patent, would satisfy the deposit requirement made herein. If a deposit has not been made under the Budapest Treaty, then in order to certify that the deposit meets the criteria set forth in 37 CFR 1.801-1.809 and MPEP 2402-2411.05, Applicant may provide assurance of compliance by affidavit or declaration, or by a statement by an attorney of record over his or her signature and registration number showing that (a) during pendency of the application, access to the invention will be afforded to the Commissioner upon request, (b) all restrictions upon availability to the public will be irrevocable removed upon granting of the patent, © the deposit will be maintained in a public depository for a period of 30 years, or 5 years after the last request or for the enforceable life of the patent, whichever is longer, (d) a test of the viability of the biological material at the time of deposit (see 37 CFR 1.807) and (e) the deposit will be replaced if it should ever become inviable.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 24-43 are under are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

7a. Claim 24, recites the limitation "the HLRRSI1" in sub-part C. There is insufficient antecedent basis for this limitation in the claim. Furthermore, the acronym HLRRSI1, renders the claim vague, because it is unclear what this acronym stands for. The instant specification defines "HLRRBMI" as "Human Leucine-Rich Repeat containing Bone Marrow-1", (see page 14, line 1), however, the acronym HLRRSI1 is not defined in the specification. It is suggested that the full name of the polypeptide be recited in the first independent claim since more than one protein might be known for the same acronym, to obviate this rejection. Appropriate correction is required.

7b. Claims 24, 39 and 43 recite "..., wherein the polypeptide has caspase modulating activity .....", however, it is unclear how is the encoded polypeptide suppose to modulate caspase activity? Does it stimulate or inhibit said capase activity?. Appropriate correction is required.

Claims 25-38, 40-42 are rejected as being vague and indefinite insofar as they depend from claim 24

Conclusion:

8. No claim is allowed.

Advisory Information:

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Fozia M Hamud whose telephone number is (703) 308-

8891. The examiner can normally be reached on Monday, Wednesday-Thursday, 6:30 am to 4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on (703) 308-4623. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Fozia Hamud
Patent Examiner
Art Unit 1647
03 November 2003

Gary L. Kunz

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